

After the genome gold rush



A field revitalized



On the track of West Nile



Beagle 2, ready by the end of the year for integration into Mars Express. But tests of Beagle 2's balloons, which cushion its landing, did not go as expected, says Rudi Schmidt, ESA's Mars Express mission manager.

At the Jet Propulsion Laboratory (JPL) here, workers are attempting to solve a similar set of daunting technical problems involving the two rovers that are the centerpiece of the \$800 million mission slated to be launched by NASA next summer. Recent tests on the airbag designed to cushion the fall proved successful, but the parachute to decelerate the speeding capsule has failed ground tests. Tests on three new parachute designs are slated for October. "If we don't have a parachute, we're not going to fly," says Chris Jones, JPL's planetary projects director.

Principal investigator Steven Squyres of Cornell University in Ithaca, New York, says he's philosophical about Mars exploration. He's confident that the NASA team will be able to solve the parachute problem and that the long-term issues will sort themselves out. Mars missions have "always been extremely difficult," he says. "But believe it or not, we have a more stable situation than anytime in the past 15 years."

—ANDREW LAWLER

With reporting by Alexander Hellemans in Naples, Italy, Judy Redfearn in Bristol, U.K., and Daniel Clerly in Cambridge, U.K.

CANCER IMMUNOTHERAPY

Select T Cells, Given Space, Shrink Tumors

Tumors normally fend off any attacks by the immune system. But now scientists have found a way to give immune cells an edge, thereby shrinking tumors throughout the body, from the skin to the liver. The work, reported online by *Science* this week (www.sciencemag.org/cgi/content/abstract/1076514), breathes life into cancer immunotherapy, a field that has struggled to achieve success in humans.

For nearly 2 decades, immunologist Steven Rosenberg and his colleagues at the National Cancer Institute (NCI) in Bethesda, Maryland, have sought to fight tumors with T cells, the immune system's first line of defense. They have extracted cells from a patient's body, selected or modified them to improve their potency, and reinfused them. But the T cells often disappeared with little effect.

Rosenberg's new protocol, which incorporates a blast of chemotherapy and a more

refined selection of immune cells than before, has had dramatically better results in a group of patients with metastatic melanoma. Although the therapy failed in some patients, in others it shriveled tumors. Of 13 volunteers, all of whom were expected to die within a few months, 10 remain alive 6 to 24 months after the first treatment.

"It's essentially what all of us have been striving for in immunotherapy," says James Mulé, an immunologist at the University of Michigan Medical School in Ann Arbor. Still, "it's really hard to predict how this will turn out" in the longer term and in larger groups of patients.

Unlike foreign intruders such as bacteria, tumor cells are the patient's own and hence are less viciously attacked by the immune system. However, the tumor surfaces of certain cancers have antigens, molecules that awaken the immune system and induce it to respond. Melanoma is one of these.

The researchers obtained tumor samples from each patient and searched for T cells that had infiltrated the tumors. Collecting as many as 50 T cell samples from a single tumor, they tested each against another tumor sample from the same patient. Rosenberg's team handpicked the two or three T cell samples that most effectively killed cancerous cells, and allowed the top T cells to multiply.

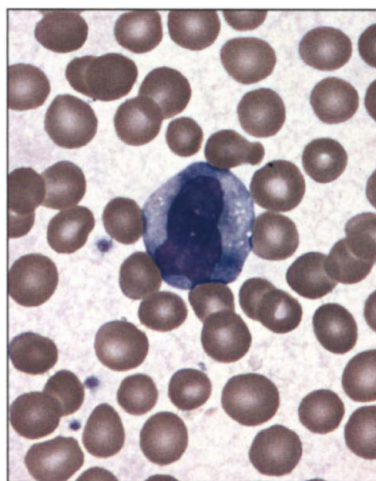
The NCI group decided that, to be effective, the selected T cells would have to make up the bulk of cells in each patient's immune system, at least temporarily, and persist long enough to act. The team administered chemotherapy to wipe out substantial numbers of existing immune cells and then reinfused the highly aggressive T cells.

Unlike many previous studies, this one not only relied on a type of T cell called a CD8 cell, which recognizes antigens and reacts, but also used CD4 cells. These "helper" T cells might have enabled the CD8 population to expand and retain its cancer-killing capacity.

In six patients, all tumors decreased in size by at least 50%. One 18-year-old remains disease-free 2 years after his treatment.

The NCI group saw some tumor shrinkage in four others. Cells infused into two middle-aged men survived at unexpectedly high levels 4 months later; in one of the men, 97% of all immune cells were, for a brief time, the type infused. "[Rosenberg's] got numbers that nobody's seen before," says Bernard Fox, an immunologist at the Earle A. Chiles Research Institute in Portland, Oregon.

Still, although the treatment reached metastases buried in the lungs and liver, it didn't work well for everyone, and Rosenberg doesn't know why. "We have an enormous effort now trying to answer that question," he says. Another challenge is monitoring side effects: Four volunteers experienced a loss of skin pigmentation, and one suffered inflammation in the eye, signs that the therapy was attacking not only cancerous cells but normal pigment-producing cells as well. And it remains unclear whether one of the therapy's successes—enabling infused cells to persist—



Top gun. A tumor-fighting T cell (center), surrounded by red blood cells, proved to be a vicious attacker of melanoma.

will have untoward effects.

Despite the hefty challenges that remain, Rosenberg and others hope this improved protocol can be adapted for other cancers and possibly even immune disorders such as AIDS. Offering infused T cells some elbowroom and handpicking only those most likely to succeed might improve the odds in battling once intractable diseases.

—JENNIFER COUZIN

BIOTERRORISM

NAS Censors Report on Agriculture Threats

When the U.S. Department of Agriculture (USDA) wanted to know if terrorists could disrupt the U.S. food supply, it turned to the National Academy of Sciences (NAS). This week, an academy panel made public its analysis—or at least most of it. Missing from the panel's report are eight hypothetical case studies that the academy excised because the material was

deemed a potential security risk.

"The academy doesn't want to provide any information that will help terrorists," says William Colglazier, the academy's executive officer, who adds that the sensitive material was removed after government officials expressed concern about a draft of the report. "The report was commissioned before 9-11, but 9-11 has changed the government's thinking on a lot of things," says Colglazier. The academy's self-censorship is the latest example



Chicken big. Terrorist attacks could force culling of millions of animals, at great cost to agricultural industries.

of a dilemma many scientific publishers face in balancing security concerns with the need for open communication.

The study, titled *Countering Agricultural Bioterrorism*, concludes that the United States is not adequately prepared to prevent or deal with attacks on agriculture. The federal government, the panel recommends, should develop a comprehensive plan for detecting and rapidly stanching outbreaks of diseases such as foot and mouth. "The potential for economic harm is enormous," says panel member David Franz of the Southern Research Institute in Birmingham, Alabama, a former head of the U.S. Army Medical Research Institute of Infectious Diseases.

USDA asked the academy early last year to examine how the nation might respond to "potential threats ... from a selected set of biological agents ... under different scenarios." But 15 months later, when a draft of the report was delivered, USDA officials had second thoughts about what they had ordered. "Their general concern was about whether the information on vulnerabilities could be exploited by terrorists," Colglazier explains. The Department of Homeland Security expressed similar concerns, he adds, and "both agencies suggested removing some material." USDA officials declined comment, although a spokesperson told *The*

New York Times last week that the agency did not request the rescissions.

None of the material is officially classified, Colglazier emphasizes, adding that NAS would not have removed the material if government officials had not objected to it. Colglazier says the academy's top officers removed eight case studies from one of the report's five chapters and put the information into an appendix. "Our intent is to give the appendix to the Administration and to Congress," he says. Everybody else, he adds, including other scientists and members of the general public, will have to settle for the edited version, which has been posted on the Web (www.nap.edu).

Franz wrote one of the excised studies, which describes how the country might respond to intentional releases of bovine spongiform encephalopathy, a deadly disease thought to be caused by infectious proteins. "We're actually pretty capable of dealing with that one," says Franz, thanks to a ban on the use of most mammalian protein in cattle feed and a surveillance program. The agent is also a lot less contagious than the virus that causes foot-and-mouth disease, he notes.

Although Franz believes that the final report retains the underlying messages from the case studies, another panelist, entomologist Marjorie Hoy of the University of Florida, Gainesville, isn't so sure. "I don't understand" why the academy would delete the case studies, she says, which drew upon publicly available information. "We were very sensitive, from the very beginning, not to provide a road map or a manual that a terrorist could follow. If you take out the case studies, that would leave a hole."

What remains are recommendations on how to prepare for an attack, including better training for farmers and other agricultural workers on how to recognize and report an outbreak. Researchers should monitor emerging diseases in other countries, the report says, and laboratories should be networked like the public health system for rapid testing of large numbers of samples. Government agencies also need to develop a clear and coordinated response plan, possibly including vaccinating herds or spraying pesticides.

The agroterrorism report is not likely to be the last time the academy will have to decide whether to make public potentially sensitive information, Colglazier says: "There's the potential for more of this. It's a different world out there."

—JEFFREY MERVIS AND ERIK STOKSTAD

High-Priority Trio The cow jumped over the moon in a children's rhyme—and now it is jumping near the front of the line of organisms due to have their genomes sequenced. The National Human Genome Research Institute (NHGRI) last week announced that the cow, the dog, and a single-celled protozoan have joined 20 other "high priority" sequencing targets—including 15 species of fungi and the honey bee (*Science*, 5 October 2001, p. 82).

The three organisms were added to the pool after one of NHGRI's periodic polls of the scientific community. The cow was blessed thanks to its usefulness in understanding human endocrinology and reproductive health. The dog has long been used to study diseases such as cancer and epilepsy. And the ciliate *Oxytricha trifallax* contains single-gene chromosomes that could help reveal the elements needed for gene regulation.

Despite the boost, the three species probably won't be sequenced immediately, because NHGRI's three U.S. sequencing centers are already busy. But the push is on to expand the capacity of existing centers and launch new ones.

Astropaleontology? An Australian geologist is NASA's choice to take over its Astrobiology Institute. Bruce Runnegar, a 61-year-old professor at the University of California, Los Angeles (UCLA), will succeed the first director, Nobel laureate and biologist Baruch Blumberg, who said last year he was stepping down from the job.

The institute is a "virtual organization" based at Ames Research Center in Mountain View, California (*Science*, 29 May 1998, p. 1338). It pulls together NASA field centers, universities, and research organizations to study the origin, evolution, and distribution of life in the universe. Runnegar currently heads UCLA's astrobiology center under contract with NASA.

Researchers say Runnegar's broad credentials—he has been a Sloan fellow in molecular evolution and has authored dozens of papers on everything from mollusk paleontology to oxygen in Earth's ancient atmosphere—will give a boost to the young, interdisciplinary enterprise. Runnegar says he'll start work at the beginning of next year.

